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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO
09/358,116	07/21/99	SACKSTEIN	R 0152.00001

EXAMINER

HM22/0718

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ART UNIT	PAPER NUMBER
1644 1644	7

DATE MAILED: 07/18/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 5/11/01

☑ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-29 is/are pending in the application.
Of the above, claim(s) 5-29 is/are withdrawn from consideration.
☐ Claim(s) ____ is/are allowed.
☑ Claim(s) 1-4 is/are rejected.
☐ Claim(s) ____ is/are objected to.
☐ Claim(s) ____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on ____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) ____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: ____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). ____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 5/11/01 (Paper No. 6), is acknowledged.
Claim 1 has been amended.

Claims 1-4 are being considered in the instant application.

Claims 5-29 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed (Paper No. 6).
The rejections of record can be found in the previous Office Action (Paper No. 5).

3. Applicant is reminded to amend the first line of the specification to update the status (and relationship) of the priority documents.

4. Applicant is reminded that the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 5

6. Claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection for the reasons of record set forth in Paper No. 5.
This is a written description rejection.

With respect to aspects of applicant's arguments as they apply to the outstanding rejection under written description; applicant's arguments, filed (Paper No. 6), have been fully considered but are not found convincing for the reasons of record.
Applicant argues that the glycoprotein is distinctly and uniquely identified by the combination of the characteristics recited in the claims, including uniquely identified by being sulfation-independent, since all other L-selectin ligands are sulfation-dependent (U.S. Patent No. 5,489,578).
Applicant further submits that the term L-selectin ligand is a term of art and is described on pages 4-6 of the instant application.

While applicant relies upon various limitations, applicant has not provided sufficient structural information that identifies the "L-selectin glycoprotein" or its "functional analogues", encompassed by the claimed invention.

The following is reiterated for applicant's convenience.

The specification broadly describes and the claims recite as part of the invention the following:

"An isolated and purified glycoprotein and functional analogues thereof characterized by being expressed on at least primitive hematopoietic cells; being a ligand for L-selectin; the binding of the ligand to L-selectin not being inhibited by anti-CD34 antibody; being resistant to O-sialogylcoprotein endopeptidase activity; not being recognized by MECA-79 a monoclonal antibody which identifies ligands of L-selectin on lymph node high endothelial venules; and being sulfation-independent"
"And functional analogues thereof".

Such "glycoprotein" and "functional analogues" do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Applicant relies upon identifying KG1a L-selectin ligand which binding activity is not sulfate-dependent utilizing an adherence assays; however applicant has not provide sufficient structural information that identifies a physiologic structure of the "L-selectin glycoprotein" or its "functional analogues", encompassed by the claimed invention.

In addition, as indicated in Sackstein et al., Blood 89: 2773-2781, 1997; applicant's own work acknowledges efforts are directed at isolating and characterizing the structure of the claimed KG1a L-selectin ligand (see entire document, including the Discussion). Here, it is noted that the structural features of the claimed KG1a L-selectin ligand remain to be determined
Also, Sackstein et al. notes that the structural determinants conferring L-selectin binding may vary in a cell and tissue-specific manner (see Abstract and Discussion). ; yet applicant has not provided such structural information.

Applicant's assertion that the material that applicant chooses to make public in a reference prior to the issuance of the patent cannot be used to limit and/or interpret the information in the non-public patent application is acknowledged.

Further, there is a lack of written description for "functional analogs"; given the absence of structural features that define the claimed "KG1a L-selectin ligand".

The specification as filed does not provide sufficient written description support for the claimed "KG1a L-selectin ligand" and "functional analogs thereof".

The skilled artisan cannot envision the claimed "L-selectin ligand" and "functional analogs thereof" in the absence of a detailed chemical structure of the "L-selectin ligand" and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. Here, defining structural features are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments are not found persuasive.

7. Claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention
This is an enablement rejection.

Applicant's arguments, filed (Paper No. 6), have been fully considered but are not found convincing for the reasons of record.
Applicant argues that the glycoprotein is distinctly and uniquely identified by the combination of the characteristics recited in the claims, including uniquely identified by being sulfation-independent, since all other L-selectin ligands are sulfation-dependent (U.S. Patent No. 5,489,578).
Applicant further submits that the term L-selectin ligand is a term of art and is described on pages 4-6 of the instant application.
Applicant's assertion that the material that applicant chooses to make public in a reference prior to the issuance of the patent cannot be used to limit and/or interpret the information in the non-public patent application is acknowledged.

The following of record is reiterated herein for applicant's convenience.

Applicant has not provided sufficient biochemical information (e.g. amino acid sequence) that distinctly identifies the claimed "KG1a L-selectin ligand" and "functional analogs thereof". While "L-selectin ligand" may have some notion of the activity of the claimed glycoprotein and applicant has relied upon the property of being sulfation-independent as well as the combination of characteristics to distinguish the instant glycoprotein from other L-selectin ligands; claiming biochemical molecules by certain functional attributes fails to enable the skilled artisan to make and use the claimed glycoprotein, without defining what the disclosed and claimed "KG1a L-selectin ligand" is made up of. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

However, the precise structural features that direct binding activity for the claimed nonconventional L-selectin ligand remains to be determined The isolation and characterization of the structure of this molecule has not been set forth, therefore the scope of the claimed isolated and purified glycoproteins functional analogs characterized by properties (a)-(e) cannot be ascertained. Again, the claimed and disclosed characteristics may have some notion of the activity of the glycoprotein as an adhesion molecule, there is insufficient precision in the claims which distinctly claims the isolated and purified glycoprotein and functional analogs thereof.

In addition, as indicated in Sackstein et al., Blood 89: 2773-2781, 1997; applicant's own work acknowledges efforts are directed at isolating and characterizing the structure of the claimed KG1a L-selectin ligand (see entire document, including the Discussion). Here, it is noted that the structural features of the claimed KG1a L-selectin ligand remain to be determined after applicant's priority dates. Here, the post-filing date reference relies upon the same or nearly the same functional characterization as that disclosed in the specification as filed and acknowledges that the KG1a L-selectin ligand has not been isolated and characterized to the point that the skilled artisan could make and use the claimed "L-selectin glycoprotein" and " functional analogs thereof" as an L-selectin ligand on primitive hemopoietic stem cells.

Here, Sackstein et al. acknowledges the existence and structural as well as functional attributes of known L-selectin ligands in distinguishing the claimed/disclosed "KG1a L-selectin ligand" (see Introduction and Discussion).

Also, Sackstein et al. Notes that the structural determinants conferring L-selectin binding may vary in a cell and tissue-specific manner (see Abstract and Discussion). ; yet applicant has not provided such structural information.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. L-selectin ligand) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects KG1a L-selectin analogs and finally what

changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. As pointed out herein, the specification as filed as well as a post-filing date reference has not provided sufficient structural or biochemical information to enable the skilled artisan to make and use the claimed KG1a L-selectin ligand. Further, I has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Because of the lack of sufficient guidance and predictability in determining which modifications would lead to "functional analogs" of the claimed/disclosed "KG1a L-selectin ligand" and "analogs thereof" and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at enabling the "KG1a L-selectin ligand and "functional analogs".

Without sufficient guidance, making and using the claimed "KG1a L-selectin ligand" and "functional analogs" thereof, including cell-l and tissue-specific L-selectin ligands is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant's arguments are not found persuasive.

8. Upon reconsideration of the patented claims set forth in U.S. Patent No. 5,403,919 and apparent availability of the MECA-79 antibody from the ATCC without restriction; the conditions for the deposit of the MECA-79 antibody under 35 USC 112, first paragraph, have been satisfied.

9. Claims 1-4: Upon consideration of the specification,; it appears that the "KG1a" cell line is required to practice the claimed invention. It appears that applicant has relied upon characterizing the "claimed KG1a L-selectin ligand" by functional screening of the KG1a cell line (see the instant specification). As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line. See 37 CFR 1.801-1.809.

Applicant's arguments, filed 5/11/01 (Paper No. 6), have been fully considered but are not found convincing for the reasons of record.

Applicant asserts that the KG1a cell line is readily available by the repeatable method set forth in the specification as filed.

In contrast to applicant's assertions, it unclear if a cell line which has the exact structural and chemical identity of the KG1a cell can be reproducibly isolated without undue experimentation. Replication of the claimed cell line an unpredictable event. Further, a particular biological cell line can undergo changes resulting in microheterogeneity. Therefore, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the

ability to practice the invention as claimed.

Applicant's arguments are not found persuasive.

10. Claims 1-4 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Sackstein et al. (Exptl. Hematol. 22: 788, 1994; Abstract 414) for the reasons of record set forth in Paper No. 5.

Applicant's arguments, filed 5/11/01 (Paper No. 6), have been fully considered but are not found convincing for the reasons of record.

Applicant argues that the prior art was published within one year of applicant's priority documents.

Applicant is reminded that the prior art was done by another and stands as prior art. See MPEP 2132.

Applicant's arguments are not found persuasive.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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July 17, 2001
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